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Cost utility analysis of monitoring osteoporosis fracture risk by a circulating microRNA based strategy compared to standard measure and no monitoring

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Tab. 1: Calculation components
<table>
<thead>
<tr>
<th>Components</th>
<th>No-monitoring</th>
<th>DXA</th>
<th>FRAX</th>
<th>microRNAs</th>
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</thead>
<tbody>
<tr>
<td>Initial population</td>
<td>138,972</td>
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<tr>
<td>Patients at risk for fracture</td>
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<td>Women over 50</td>
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<td>Men over 50</td>
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<td>Women without fractures</td>
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<td>Men without fractures</td>
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<td>Women with fractures</td>
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<td>Men with fractures</td>
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<tr>
<td>Women at risk for hip fracture</td>
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<td>Men at risk for hip fracture</td>
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<tr>
<td>Women at risk for vertebral fracture</td>
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<td>Men at risk for vertebral fracture</td>
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<tr>
<td>Women at risk for other fracture</td>
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<td>Men at risk for other fracture</td>
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Objectives
Due to its prevalence worldwide, osteoporosis is considered a serious public health concern with over 200 million patients worldwide, not limited to, but most prevalent in postmenopausal women. In Austria 393,000 women are affected, 89,200 with a prior fracture. Bone-mineral-density (DXA) and the Fracture-Risk-Assessment-Tool (FRAX) are considered to be the standard measure for fracture risk assessment. MicroRNAs have recently emerged as important factors in bone physiology and specific blood-circulating microRNAs have been suggested as biomarkers for osteoporosis. The osteoMRix™ test is a novel diagnostic device for processing of fracture risk. The purpose of this analysis was to estimate the cost-effectiveness of osteoporosis fracture-risk monitoring for treatment decisions using either microRNA, DXA, FRAX or no monitoring in women without prior fracture.

Methods
A Cost-Utility-Model was developed to simulate long-term consequences of osteoporosis in females from age 50 over lifetime. Markov-modeling techniques were used to estimate fracture-incidence according to risk-groups. If women were monitored they follow the case finding strategy from the National Osteoporosis Guideline Group 2008 and were split in 3 risk-categories (high, intermediate, low). High-risk patients receive medical treatment, with the consequence of risk reduction. Each year a patient has a probability of suffering a fracture, remaining healthy, or deceasing. If the patient incurs a fracture she will move to the health state “fracture”. This health state is subdivided on fracture type: hip, vertebral, wrist/forearm or other osteoporotic fractures. In the next Markov cycle the patient may experience a recurrent fracture or move to the “post fracture” state or die. The cycle length is 1 year (cycle correction was implemented) and all patients are followed through the model from age 50 over lifetime. QALYs (utility values from the literature), life-years (LYs) and costs were discounted (3% p.a).

Clinical Data
Distribution of the number of clinical risk factors (CRF) among age groups were estimated based on Austrian BML data. The fracture risk of a female of age 50 and age group 80+ of CRF is documented by Compton et al. (2009). Based on the number of total fractures the distribution of the number of CRFs were calculated. The sensitivity of the different monitoring strategies were derived from literature. Risk Reduction due to osteoporosis drug treatment was obtained from a NICE publication, which includes sixteen reviews of individual pharmacological interventions.

Resource Use (RU) and Costs
Monitoring is considered as described:
- no monitoring: in the no monitoring arm receive no regular monitoring. In case of a fracture patients were monitored with DXA every 2 years.
- DXA: Women without fractures were monitored from age 65, every 2 years. Women with a fracture were also monitored with DXA before age 65.
- FRAX: In the FRAX arm women were monitored with FRAX yearly from age 50 according the case finding strategy from the National Osteoporosis Guideline Group 2008. Women in the high risk group were treated.
- microRNAs: Women were monitored yearly from age 50. Women with high risk were treated. After a fracture women were monitored with DXA.

RU due to fractures were derived from a retrospective chart review which IPF has conducted in the year 2010. A sample of 166 of female osteoporosis patients with a low energy fracture (mean age 76 years) was assessed by random sampling (according to defined in- and exclusion criteria) in seven Austrian centers. Direct medical costs comprise all treatment costs due to osteoporosis after fracture (Table 1). The RU based on medical records were collected for a follow up of 1 year.

The percentage of pharmacologically treated patients were estimated based on Austrian publication (Dimai et al. 2012) and the market share of medication was derived from IMS data. Outpatient costs were derived from the tariff catalogues from all 9 regional health insurance companies. Inpatient costs are calculated on the Austrian diagnosis related groups (DRGs) refunding (-LKP System) and medication costs were extracted from the Austrian official price list. All costs represent data from 2015 and were discounted with 3%.

Sensitivity Analysis
Deterministic and probabilistic sensitivity analysis was carried out. Fig. 2 displays the deterministic sensitivity analysis.

Results
Life-time costs in the microRNA biomarker-arm amount to 9,409€ and 19,389 QALYs (35.252 Ly). Costs associated with the DXA-strategy are 9,353 € and 19,384 QALYs (35.245 Ly). The incremental-cost per QALY gained (ICER) vs. DXA was 10,404 €. Costs associated with the FRAX-strategy are 9,501 € and 19,385 QALYs (35.25 Ly). MicroRNAs dominate FRAX. Life-time cost without monitoring amount to 9,189 € and 19,376 QALYs (35.235 Ly). The ICER vs. no-monitoring was 17,038 €.

Monte Carlo probabilistic sensitivity analysis, results of 500 trials plotting incremental cost versus incremental effects, demonstrated that osteoporosis monitoring with microRNA was cost effective compared to comparator strategies.

References
Bones (2015) WHO FRAX®, a using either microRNAs, DXA, FRAX or no monitoring to evaluate fracture risk and risk assessment. MicroRNAs have recently emerged as important factors in bone physiology and specific blood-circulating microRNAs have been suggested as biomarkers for osteoporosis. The osteoMRix™ test is a novel diagnostic device for processing of fracture risk. The purpose of this analysis was to estimate the cost-effectiveness of osteoporosis fracture-risk monitoring for treatment decisions using either microRNA, DXA, FRAX or no monitoring in women without prior fracture. The ICER of microRNA vs. no monitoring reach from 545,665 € to -11,124 €. ICER of microRNA vs. DXA are between 61,410 € and -35,279 €. A comparison of microRNA vs. FRAX shows that osteoporosis monitoring with microRNA vs. FRAX is cost-effective or becomes cost-saving in all variations of the sensitivity analyses.

Monte Carlo probabilistic sensitivity analysis, results of 500 trials plotting incremental cost versus incremental effects, demonstrated that osteoporosis monitoring with microRNA was cost effective compared to comparator strategies.

MicroRNAs is cost-effective against no monitoring in more than 95% of simulations with a willingness-to-pay-value up to 10,000 €; in 97% compared to DXA and more than 98% compared to FRAX (Fig. 3).

Conclusion
Fracture-risk assessment using microRNAs dominates FRAX-strategy and is a cost-effective alternative vs. DXA and no-monitoring.

References